

*The pending claims are presented below:*

**1-113. Cancelled**

**114. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from periodontal disease, comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less.

**115. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from periodontal disease, comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

**116. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from periodontal disease, comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light

chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

**117. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from periodontal disease, comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is D2E7.

**118. (Previously Presented)** A method for treating a subject suffering from periodontal disease, comprising administering to the subject an antibody such that the periodontal disease is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $k_d$  of  $1 \times 10^{-8}$  m or less and a  $k_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC $_{50}$  of  $1 \times 10^{-7}$  m or less.

**119. (Previously presented)** A method for treating a subject suffering from periodontal disease, comprising administering to the subject an antibody such that the periodontal disease is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

**120. (Previously presented)** A method for treating a subject suffering from periodontal disease, comprising administering to the subject an antibody such that the

periodontal disease is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

121. **(Previously presented)** A method for treating a subject suffering from periodontal disease comprising administering to the subject an antibody such that the periodontal disease is treated, wherein the antibody is D2E7.

122-140. **(Canceled)**

141. **(Previously Presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject both an antibody and methotrexate, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human  $\text{TNF}\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human  $\text{TNF}\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-7}$  M or less.

142. **(Previously presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject both an antibody and methotrexate such that the rheumatoid arthritis is treated, wherein the antibody is D2E7.

143. **(Previously presented)** A method for inhibiting human  $\text{TNF}\alpha$  activity in a human subject suffering from obesity comprising administering to the human subject an antibody such that human  $\text{TNF}\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human  $\text{TNF}\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human  $\text{TNF}\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-7}$  M or less.

**144. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from obesity comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

- a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

**145. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from obesity comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

**146. (Previously presented)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from obesity comprising administering to the human subject an antibody such that human TNF $\alpha$  activity in the human subject is inhibited, wherein the antibody is D2E7.

**147. (Previously Presented)** A method for treating obesity in a subject suffering from obesity comprising administering to the subject an antibody such that obesity is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8} \text{ m}$  or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and

neutralizes human  $\text{TNF}\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-7}$  M or less.

**148. (Previously presented)** A method for treating obesity in a subject suffering from obesity comprising administering to the subject an antibody such that obesity is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

- a) dissociates from human  $\text{TNF}\alpha$  with a  $K_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

**149. (Previously presented)** A method for treating obesity in a subject suffering from obesity comprising administering to the subject an antibody such that obesity is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

**150. (Previously presented)** A method for treating obesity in a subject suffering from obesity comprising administering to the subject an antibody such that obesity is treated, wherein the antibody is D2E7.

**151. (Previously presented)** A method for inhibiting human  $\text{TNF}\alpha$  activity in a human subject suffering from radiation toxicity comprising administering to the human subject an antibody such that human  $\text{TNF}\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof,

that dissociates from human  $\text{TNF}\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human  $\text{TNF}\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-7}$  M or less.

152. **(Previously presented)** A method for inhibiting human  $\text{TNF}\alpha$  activity in a human subject suffering from radiation toxicity comprising administering to the human subject an antibody such that human  $\text{TNF}\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

- a) dissociates from human  $\text{TNF}\alpha$  with a  $K_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

153. **(Previously presented)** A method for inhibiting human  $\text{TNF}\alpha$  activity in a human subject suffering from radiation toxicity comprising administering to the human subject an antibody such that human  $\text{TNF}\alpha$  activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

154. **(Previously presented)** A method for inhibiting human  $\text{TNF}\alpha$  activity in a human subject suffering from radiation toxicity comprising administering to the human subject an antibody such that human  $\text{TNF}\alpha$  activity in the human subject is inhibited, wherein the antibody is D2E7.

155. **(Previously Presented)** A method for treating radiation toxicity in a subject suffering from radiation toxicity comprising administering to the subject an antibody such that radiation toxicity is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  m or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC $_{50}$  of  $1 \times 10^{-7}$  m or less.

156. **(Previously presented)** A method for treating radiation toxicity in a subject suffering from radiation toxicity comprising administering to the subject an antibody such that radiation toxicity is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3}$  s $^{-1}$  or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

157. **(Previously presented)** A method for treating radiation toxicity in a subject suffering from radiation toxicity comprising administering to the subject an antibody such that radiation toxicity is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

158. **(Previously presented)** A method for treating radiation toxicity in a subject suffering from radiation toxicity comprising administering to the subject an antibody such that radiation toxicity is treated, wherein the antibody is D2E7.

159. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $5 \times 10^{-4} \text{ s}^{-1}$  or less.

160. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-4} \text{ s}^{-1}$  or less.

161. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-8} \text{ M}$  or less.

162. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-9} \text{ M}$  or less.

163. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-10} \text{ M}$  or less.

164. **(Previously presented)** The method of claim 141, wherein the isolated human antibody, or antigen-binding portion thereof, is a recombinant antibody, or antigen-binding portion thereof.

165. **(Previously Presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject both an antibody and methotrexate, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ



ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

166. **(Previously presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject both an antibody and methotrexate, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.